REMARKS

In the Official Action Dated August 11, 2008, the Office rejected various claims under 35 U.S.C. § 112, §102(b) and §103(a).

In this paper, Applicants have responded to each of the claim rejections.

For purposes of expediting prosecution, Applicants have cancelled 7-8, and 19-29, and amended claims 9 and 30-32. Applicants have also cancelled claims 33-38 as being directed to a non-elected invention.

These amendments are all supported by the specification as filed. No new matter has been added. Applicants preserve the right to file continuing patent applications on any subject matter that has been cancelled from the claims, including any cancelled claims.

Claim Objections

The office objected to claim 32, alleging that claim 32 is in improper form because a multiple dependent claim cannot depend on another multiple dependent claim.

In response to this claim objection, Applicants have amended claim 32 to make it depend only on claim 1. Accordingly, this objection has been obviated and Applicants respectfully request reconsideration and withdrawal of this objection.

Rejections under 35 U.S.C. § 112, 1st Paragraph

The Office rejected claims 1-9 and 30-31 under 35 U.S.C. § 112, first paragraph, alleging that the term "prodrug" is not enabled.

For the sole purpose of expediting prosecution, Applicants have deleted the term "prodrug" from the claims, thereby rendering this rejection moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection. Applicants respectfully request reconsideration and removal of this rejection under 35 U.S.C. § 112, 2nd Paragraph.

Rejections under 35 U.S.C. § 112, 2nd Paragraph

The Office rejected claim 30 under 35 U.S.C. § 112, first paragraph, alleging that compound # 16 does not fall within the genus of formula I in claim 1.

In response, Applicants have amended claim 30 into an independent claim. Accordingly, this rejection has been obviated. Applicants respectfully request reconsideration and removal of this rejection under 35 U.S.C. § 112, 2nd Paragraph.

Rejections under 35 U.S.C. § 102(b)

(1) The Office has rejected claim 1 under 35 U.S.C. § 102(b), alleging that these claims are anticipated by Lee et al., U.S. Patent 5,436,233. Applicants respectfully traverse this rejection.

Applicants have cancelled claim 1, rendering this rejection moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

(2) The Office has rejected claim 1 under 35 U.S.C. § 102(b), alleging that this claim is anticipated by Lee et al., (J. Med. Chem.). Applicants respectfully traverse this rejection.

Applicants have cancelled claim 1, rendering this rejection moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

(3) The Office has rejected claim 1 under 35 U.S.C. § 102(b), alleging that this claim is anticipated by Chen et al., (U.S. Patent No. 4,306,065). Applicants respectfully traverse this rejection.

Applicants have cancelled claim 1, rendering this rejection moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

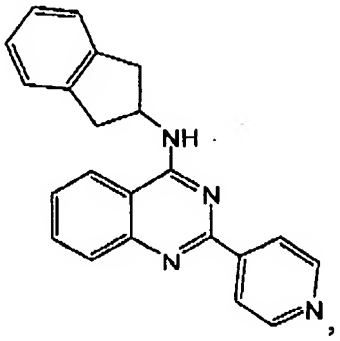
(4) The Office has rejected claims 1-6 under 35 U.S.C. § 102(b), alleging that this claim is anticipated by Matsuno et al., (WO 02/051836). Applicants respectfully traverse this rejection.

Applicants have cancelled claims 1-6, rendering this rejection moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

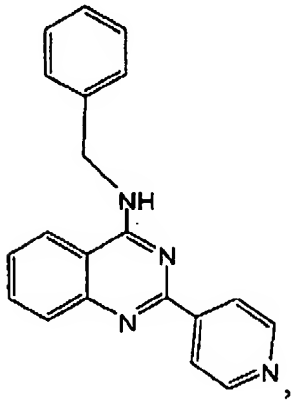
Rejection under 35 U.S.C. § 103(a)

The Office has rejected claims 1-9, 30 and 31 U.S.C. § 103(a), alleging that these claims are unpatentable over Lee et al. in view of Gibson et al. Applicants respectfully traverse this rejection.

The Office's reasoning for alleging a *prima facie* case of obviousness is that the Applicants' elected the following species



Lee teaches the following compound in example 3(q)



and Gibson et al. discloses that the indanyl moiety in the 4-position of the quinazoline possessed comparable biological properties.

In response to the Office's reasoning, Applicants stress that, firstly, Applicants elected compound is chemically distinct and structurally not obvious to example 3(q) in Lee et al. Applicants' elected compound contains a more bulky fused bicyclic moiety directly bonded to nitrogen, wherein example 3(q) in Lee et al. contains a smaller phenyl group, which not only differs from Applicants' elected species in bulk and electronic charge distribution, but also differs in that it is attached to the nitrogen atom via a methylene linker. These structural differences between these two compounds are substantial, and the skilled artisan would suspect that the chemical behavior of these two compounds may differ.

Furthermore, Lee et al. teaches compounds that inhibit cGMP phosphodiesterase, which is an entirely different enzyme and target than Tie-2 kinase, which Applicants' compounds inhibit. Accordingly, one skilled in the art would not have had any reason to

look at Lee et al. for making compounds that can inhibit Tie-2 kinase, which are Applicants' compounds. Further, one skilled in the art would not have a reasonable expectation of success that modifying the compounds in Lee et al., which inhibit cGMP phosphodiesterase, would result in compounds that inhibit Tie-2 kinase. Moreover, the indications that are implicated when cGMP phosphodiesterase is inhibited are metabolic disorders, and are not related to cancer. In contrast, the indications implicated when Tie-2 is inhibited are cancer related disorders, and are not related to metabolic related disorders. The compounds disclosed in Lee et al. therefore do not have comparable biological properties as Applicants' compounds, since the compounds in Lee et al. inhibit cGMP phosphodiesterase, which is an entirely different enzyme and target than the Tie-2 kinase, which Applicants compounds inhibit.

Gibson et al. disclose compounds that inhibit Epidermal Growth Factor Receptor, which is a different target than both Tie-2 and cGMP phosphodiesterase. The compounds in Gibson et al. are structurally further removed from Applicants' compounds because none of these compounds disclose the pyridine moiety attached to the quinazoline moiety, as is required by Applicants claims. Accordingly, Neither Lee et al. or Gibson et al. disclose or suggest, either alone or in combination, any articulated reasoning with some rational underpinning to support that the instant claims would have been obviousness to one skilled in the art.

In regard to claim 30, claim 30 has been amended and is now in independent form. Neither Lee et al. or Gibson et al., either alone or in combination, provide any articulated reasoning to the skilled artisan to modify the compounds in these cited articles to come up with any of the specific compounds in claim 30 with the exact arrangement of atoms that each of these claimed compounds have. Also, there was no reasonable expectation of success that modifying the compounds in Lee et al., for the reasons stated above, to arrive at any of the compounds in claim 30.

Since Lee et al. and Gibson et al., either alone or in combination, fail to support a legal conclusion that the instant claims would have been *prima facie* obvious for reasons stated above, Applicants respectfully request reconsideration and withdrawal of this rejection.

In view of the foregoing amendments and remarks, Applicants respectfully submit that the present application is in condition for allowance, which action is earnestly solicited.

Since generic claim 9 is now in a form for allowance, Applicants respectfully request the Examiner to allow claims 10-18 and 31, which are all claims that are dependent on generic claim 9.

A one month extension of time is believed to be due in order to process this document and any paper attached. Should the U.S. Patent Office determine that an additional fee and/or other relief is required at this time, the Commissioner is authorized to charge the cost of such relief and/or fees to Deposit Account No. 50-1108, referencing EX04-019C-US.

Respectfully submitted,

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